FORMULATION AND EVALUATION OF GENTAMYCIN SULPHATE OPTHALMIC NANOEMULGEL

A synopsis submitted
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Doctor of Philosophy

In

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by

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DECLARATION

I hereby declare that the work presented in this report entitled **"FORMULATION AND EVALUATION OF GENTAMYCIN SULPHATE OPTHALMIC NANOEMULGEL"**, will be carried out by me.

I have given due credit to the original authors/sources for all the words, ideas, diagrams, graphics, computer programs, experiments, results, that are not my original contribution. I have used quotation marks to identify verbatim sentences and given credit to the original authors/sources.
I affirm that no portion of my work is plagiarized, and the experiments and results reported in the report are not manipulated. In the event of a complaint of plagiarism and the manipulation of the experiments and results, I shall be fully responsible and answerable.

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CERTIFICATE

Certified that **SURAJ MANDAL** has carried out the research work presented in this synopsis entitled **"FORMULATION AND EVALUATION OF GENTAMYCIN SULPHATE OPTHALMIC NANOEMULGEL"** for the award of **Doctor of Philosophy (Pharmaceutical Sciences)** from IIMT College of Medical Sciences, IIMT University, Ganga nagar, Meerut under **Dr. Nitin Kumar** supervision. The synopsis embodies results of original work, and studies are carried out by the student herself and the contents of the synopsis do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University/Institution.

Signature
Dr. Nitin Kumar
(Professor)

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CHAPTER – 1

INTRODUCTION

An emulsion is a dispersion system consisting of finely dispersed droplets in a non-agitated vehicle. Macroemulsions (droplets with a diameter of 1 to 100 µm) are also referred to as conventional emulsion/colloid, emulsion types are classified according to the droplet. generally unstable in water droplets or nearly buoyant with one and a half parts dispersion, readily absorbed by solid particles on the surface. While microemulsions (droplets between 10-100nm) are an isotropic liquid system with more uniform size and physical properties and a thicker nanoemulsion (droplet diameter 20-200nm). Nanoemulsion gel is known as nanoemulsion-based hydrogelation by adding an integrated nanoemulsion system to the hydrogel matrix, which provides better skin penetration.[1]

1.1. Nanoemulsion to nanoemulgel

The nanoemulsion technology is the best drug delivery approach to maximise potency and minimise toxicity for most pharmaceuticals. To help them in their hunt for novel and complex dose forms, researchers studied the straightforward administration of medications. A suitable surfactant or co-surfactant with an acceptable HLB value is added to the two immiscible liquids (oil and water) to create a homogenous solution, which is what the nanoemulsion system is made of. Between 10 and 100 nm is where this thermodynamically stable system is located. The many compartments of a stabilised nanoemulsion are depicted in Figure 1.1. By speeding up the processing of medications in the target area and enhancing their absorption through the skin, nanoemulsion is a viable option for targeting poorly soluble pharmaceuticals and improving the penetration of drug delivery systems.[2]

The physical characteristics of an emulsion are unaffected by the actions of a nanoemulsion that contains nanoscale spheres. However, it has been proven that the therapeutic as a whole is bioavailable. Since first pass metabolism is prevented, it makes sense that the transdermal bioavailability of lacidipine has been studied 3.5 times more than with oral medication. Additionally, nanoemulsion enhances drug penetration through the skin, which engages the interests of researchers. Additionally, the more medication that can be added to the mixture, which

improves the thermodynamics towards the skin, the smaller the particle size. Skin penetration is improved by the medication's affinity for partitioning. Nile red (NR) dye loaded in lecithin nanoemulsion was reported to enter the skin 9 times more effectively than NR-loaded general emulsion in one study. Ethyl oleate and propylene glycol, two other ingredients in the mixture, also encourage permeability. Transdermal medication distribution is most severely hindered by the stratum corneum, a tissue layer that is 10–20 mm thick and has a well-organized, well-composed lipid/protein matrix. The bioavailability of lipophilic flurbiprofen in nanoemulsion is increased by 4.4 times when applied topically compared to oral dosage, according to a recent study.[3]

Because of this, the nanoemulsion is a spontaneous emulsifying technique that performs better than polymeric nanoparticles and liposomes in many respects, including cheaper guidance costs, more hydrophilic and lipophilic drug loading systems, and longer shelf lives while healing agents are conserved.

1.2. Nanoemulgel:

The introduction of a nanoemulsion that is wholly based on hydrogel is made possible by the incorporation of the nanoemulsion machine intergraded into the hydrogel matrix, or nanoemulgel. Skin penetration is enhanced consequently. Scientists have concentrated their efforts on this nanoemulgel combination in order to develop several drugs that may be used to treat a variety of skin disorders.

As demonstrated in Table 1, emulgel is not a brand-new formulation type and is currently available on the market.

Table 1.1: Emulgel product available on the market today

S. N.	Product Name	Manufacturer	Active Ingredients
1	Reumadep Emulgel	ErbozetaEnergia Verde	Arnica, Ashwagandha, Myrrh, Ginger, Rosemary, Cloves, Mint.

2	Emulgel Levorag Monodose	THD LAB Farmaceutici	
3	Voltaren Emulgel	Novartis Consumer Health	Propylene glycol, 100 g Diclofenac diethylamine equivalent to 1 g diclofena sodium Base: An aqueous gel fatty emulsion containing isopropanol and propylene glycol.
4	Meloxic Emulgel	Provet	Meloxicam
5	Coolnac Gel Emulgel 1 %	Chumchon	Diclofenac Diethylammonium
6	Benzolait AzEmulgel	Rordermal	Benzoylperossido 10%
7	Miconaz-H-emulgel	Medical Union Pharmaceuticals	Miconazole nitrate, Hydrocortisone
8	Voveron Emulgel	Novartis Pharma	Diclofenac diethyl amine
9	Diclobar emulgel	Barakat pharma	Diclofenac diethyl amine
10	Levorag emulgel	THD Ltd	Hibiscus, liqourice and natural extracts

The nanoemulgel formulation of the topical delivery system acts as a drug reservoir, influencing the rate at which drugs are delivered to the skin from the internal phase. These release processes are influenced by the network's polymer chain composition and crosslink density.[4] Furthermore, a drug's ability to penetrate the skin and successfully release the therapeutic agent is determined by its ability to diffuse out of the vehicle and penetrate through the barrier.

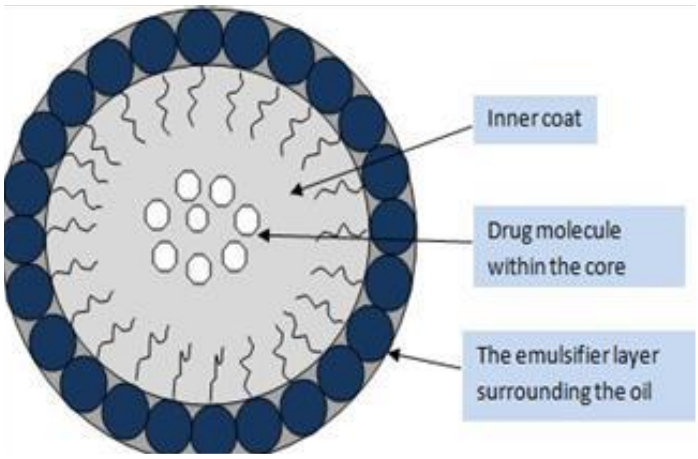


Figure 1.1: Diagram of Stabilized Nanoemulsion.

The insertion of a nanoemulsion system intergraded into gel matrix results in the formation of nanoemulgel, which incorporates nanoemulsion in a gel basis and increases skin penetration.[5] The mixing of nanomulgels, which serve as drug reservoirs, affects drug release from the inner to the outer phase and beyond. When nanoemulgel is applied to healthy skin, oil droplets are produced, which move through the skin's SC and transport medicine to the desired location. The medication's increased solubilization in the oil phase results in a wider concentration gradient toward the skin, which improves drug penetration into the skin. Nanoemulsion gels attach very effectively. Patient compliance is strengthened further by the higher sparing ability in comparison to creams and ointments and the lower stickiness.

1.3. Advantage: Nanoemulgels have several advantages over other topical formulations that have been researched, including the following:[6-7]

a) Avoid first pass metabolism.
b) Patient-friendly.
c) Appropriate for self-medication.
d) Offer local medicine delivery services.
e) Simple medication discontinuation.
f) Easily suitable for the surroundings surrounding skin.
g) Established effectiveness for a sustained and regulated medication delivery method.
h) The nanoemulsion's stability is influenced by the drug's affinity for the oil, which is enhanced by the dispersion of oil droplets in the gel basis.

i) A strong concentration gradient that increases medication penetration as it descends is also produced by a strong solubilizing power and good skin adhesion.
j) These formulations also improve patient compliance and aid in the distribution of lipophilic and insufficiently water-soluble medications.
k) Furthermore, the nanoemulgel facilitates regulated, shorter-half-life drug release.
l) Provide a formulation that is easier to spread than creams.
m) Nanoemulgels are both non-toxic and non-irritating.

CHAPTER – 2

LITERATURE REVIEWS

1.1. Nanoemulsion:

i. **Singh Y. *et al.* (2017);** Recall that an ampiphillic surfactant stabilises either water in oil (W/O) or oil in water (O/W) droplets to produce a biphasic dispersion known as a nanoemulsion. These seem to be ultrafine dispersions with changeable drug loading, viscoelastic properties, and aesthetic attributes that may be used for a variety of activities, including drug administration.[8]

ii. **Halnor V.V. *et al*. (2017);** argues that nanoemulsions are clear, isotropic, thermodynamically stable liquid mixes of oil, water, surfactant, and co-surfactant. Nanoemulsions typically have droplet widths between 20 and 200 nanometers. The size and form of the particles scattered in the continuous phase of a nanoemulsion is the key property that separates an emulsion from a nanoemulsion. Nanoparticles are not present in an emulsion. This strategy aims to address a number of issues with traditional pharmaceutical administration, including noncompliance and insufficient bioavailability.[9]

iii. **Gupta A. *et al*. (2016);** Stated A kind of liquid-in-liquid dispersion known as a nanoemulsion is kinetically stable and has a dimension of fewer than 100 nanometers. Numerous industries, including those involved in the distribution of foods, beverages, cosmetics, and pharmaceuticals as well as those that manufacture materials, employ nanoemulsions. They don't seem to have any impact on how light travels through them. Both more conventional techniques, such bubble bursting, and more contemporary ones, including high pressure homogenization, ultrasonication, phase inversion temperature, and emulsion inversion point, may be used to create nanoemulsions.[10]

1.2.Nanoemulgel

i. **Rehman A. *et. al.*, (2022):** In this specific piece of research, the goal was to construct nanoemulgels loaded with eucalyptol in order to improve wound healing and then analyse them both in vitro and in vivo. This was done so that the results could be used to future work. Nanoemulsions were produced by mixing an aqueous phase with an oil phase, and the technique used to do so was known as solvent emulsification diffusion. After that, a nanoemulgel was produced by mixing nanoemulsions with a gelling agent (Carbopol 940)

at a ratio of 1:1. This resulted in the formation of the nanoemulgel. The development of the nanoemulgel was the end outcome of this process. The nanoemulgels were evaluated for their spreadability, polydispersity index (PDI), drug content, stability, homogeneity, pH, and viscosity, as well as in vitro and in vivo testing for drug release.[11]

ii. **Yeo E. *et. al.*, (2021):** Phases of the nanoemulsion were determined by a solubility research, and the oil, surfactant, and cosurfactant ended up being a mixture of Capryol 90 and tocotrienols, Solutol HS15, and Transcutol P. Nanoemulsions were produced by the spontaneous emulsification technique. Similar nanoemulgels were produced by combining the improved nanoemulsions with carbopols. The globule size, polydispersity index (PDI), surface charge, viscosity, mucoadhesive property, spreadability, in vitro release, and release mechanism were all measured in order to determine whether or not the optimised nanoemulgels were thermodynamically stable.[12]

iii. **Morteza-Semnani K**. ***et. al.*, (2021):** Essential oils increase transdermal permeability safely. Water insolubility limits their utilisation. Nanotechnology may circumvent this constraint. This study investigated whether cumin essential oil increased the transdermal permeability of nanoemulgel formulations containing diclofenac sodium. Cumin essential oil was nanoemulsified by high-pressure homogenization. Tween 20, Tween 80, and Span 80 were used to alter HLB values from 9.65 to 16.7 to optimise the formulation. Preparations had droplet size, polydispersity index, and zeta potential. Mixing an essential oil nanoemulsion at 2 and 4% concentrations with a 0.75 percent Carbopol gel matrix yielded a nanoemulgel formulation. Franz diffusion cells assessed nanoemulgel penetration. Thermal (tail-flick) and chemical (formalin) mouse models were used to examine the formulations' antinociceptive capabilities. The lowest particle size was 9.65 HLB (82.20 5.82 nm). After 24 hours, the nanoemulgel penetrated diclofenac at 34.75 1.07 g/cm2 from 28.39 1.23. Commercial products (22.97 1.92 g/cm2) and formulations containing essential oils (21.18 2.51 g/cm2) penetrated better than the basic gel. In formalin and tail-flick tests, diclofenac nanoemulgel with essential oil beat plain gel and commercial formulations in antinociception. The study suggests using nanoemulgel cumin essential oil as a skin enhancer to boost drug efficacy.[13]

1.3.Methodology of nanoemulgel

i. **Bhardwaj S. *et. al.*, (2022):** The TC-based nanoemulsions were produced by high-pressure homogenization and afterwards evaluated for a number of in vitro characteristics. Thus, the optimised nanoemulsions were used to make NEG.[14]

ii. **Algahtani MS**. ***et. al.*, (2022):** To improve topical dispersion and stability, the present endeavour attempts to encapsulate retinyl palmitate in nanoemulsion and then combine it with a hydrogel system. Low-energy emulsification method was used to nano-encapsulate retinyl palmitate. The study and formulation optimization were done using phase behaviour research.[15]

iii. **Ahmad J. *et. al.* (2019);** Ahmad J. *et. al*. utilizing a low-energy emulsification strategy was the method of choice for the development of the thymol-loaded nanoemulgel formulation that was to be used as a topical therapy for acne in the current investigation. In addition, the newly developed formulation was tested for its thermodynamic stability, in addition to having its mean droplet size, zeta potential, drug content, and in-vitro drug diffusion study outcomes evaluated.[16]

iv. **Anand K. *et. al.* (2019);** Said that the nanoemulgel formulation is an emulsion-based gel used topically. Nano-sized globules of emulsion may be created using high-energy or low-energy methods, and then an appropriate gelling agent can be added to turn them into nanoemulgel. Nanoemulgels need a wide variety of polymeric components, in addition to several surfactants and fatty compounds, for their production. Their globule sizes may range from 5 to 500 nm, and they can come from natural, synthetic, or semi-synthetic sources.[17]

1.4.Nanoemulsion of ophthalmic delivery system

i. **Yang J. *et al.* (2022):** Although luciconazole (LCZ), a brand-new imidazole medication, offers powerful and broad-spectrum antifungal activities that make it a viable treatment for fungal keratitis, its low solubility prohibits it from being prescribed for ocular infections. Liconazole is an example of an imidazole drug (LCZ). The central composite design-response surface technology may boost bioavailability after topical administration to the eye, according to this study's investigation. Additionally, it created and improved LCZ nanoemulsion formulations (LCZ-NE). Water, Capryol 90, ethoxylated hydrogenated castor oil, and Transcutol® P made up the LCZ-NE formulation. The LCZ-NE droplet appeared spherical and homogeneous with a size of 18.43 0.05 nm and a polydispersity

index of just 0.070 0.008. An in vitro investigation on the release of LCZ revealed that the LCZ-NE released more of the medication than an LCZ solution did (LCZ-Susp). Increases in the inhibitory zone revealed that the LCZ-antifungal NE's effectiveness had greatly increased when tested in vitro. The impact of the LCZ-ocular NE on rabbit eyes was studied, and it was shown that rabbit eyes could efficiently tolerate the discomfort. An examination of the ocular pharmacokinetics revealed that entire eye tissues treated with LCZ-NE had a greater bioavailability than tissues treated with LCZ-Susp. In conclusion, the new LCZ-NE formulation showed outstanding physicochemical qualities, tolerable side effects, better antifungal activity, and increased bioavailability in eyes.[18]

ii. **Prajapati BG. *et al.* (2022):** The present study's objectives included developing an in situ moxifloxacin hydrochloride nanoemulsion gel for ocular injection and assessing the possibility of ocular irritation and diffusion. The in situ gel was produced by processing nanoemulsions made using the water titration procedure. The physical and chemical characteristics of the formulations as well as their in vitro drug release were evaluated based on the formulations that had the best gelation temperature. The best nanoemulsion in situ gel was selected to study its surface shape, sterility, isotonicity, and ocular irritancy. The enhanced formulation's average droplet size and polydispersity index were 28.29 nm and 0.221 nm, respectively. The surface form and physicochemical properties were also found to be within the acceptable range for ocular administration. With an overall drug release of 84.59% over the course of 12 hours, the formulation showed sustained drug release. The ocular irritancy test revealed that the optimal formulation was well tolerated by the eyes. These findings demonstrated the potential of in situ nanoemulsion-based ophthalmic therapy for the treatment of eye diseases.[19]

1.5.Gentamycin Sulphate:

i. **Bulman ZP**. ***et al.*** **(2020):** Gentamicin is a medicine that is made up of many different parts, many of which have not been tested on their own for safety and effectiveness. On the other hand, most drugs are dosed as single components and require strict characterizations of trace impurities. Most of gentamicin is made up of the four compounds C1, C1a, C2, and C2a. These compounds are called gentamicin congeners.[20]

ii. **Umeyor C. *et al.* (2016):** In order to create self-nanoemulsifying formulations (SNEFs) structured with PEG 4000 as PEGylated SNEFs, rational blends of soybean oil, a

combination of Kolliphor1 EL and Kolliphor1 P188 as surfactants, and Transcutol1 HP as a co-surfactant were used. These formulations were then tested for oral delivery of gentamicin. The initial area of the nanoemulsion produced by the water titration approach using oil, surfactant combination, and cosurfactant was reduced with the addition of gentamicin and PEG 4000. Emulsion droplets were between 80 and 210 nanometers in size (nm).[21]

iii. **Dozzo P. *et al.* (2010):** Aminoglycosides may have an impact on bacteria by permanently adhering to divalent cations. By attaching to the highly conserved A-site of the bacterial 16 S subunit of 30 S rRNA, they may also stop the normal production of proteins.[22]

iv. **Abdelbary G. *et al.* (2008):** The purpose of this research was to see whether it was feasible to use non-ionic surfactant vesicles to safely give gentamicin sulphate, a local antibiotic that is water soluble, to the eye (niosomes). Niosomal formulations were developed using a number of surfactants (Tween 60, Tween 80, or Brij 35), cholesterol, a substance known as dicetyl phosphate (DCP), a negative charge inducer, and a thin film hydration procedure.[23]

1.6. Oils

i. **Shehata TM. *et al.* (2022):** The objective of the present study was to examine the role of eucalyptus oil, a specific natural essential oil, as an anti-inflammatory agent and to determine if it may enhance the anti-inflammatory effects of meloxicam. This topical nanoemulgel formulation, according to our research, is the first to include both meloxicam and eucalyptus essential oil. Meloxicam was first formulated in a eucalyptus oil-based nanoemulsion formulation. A 22 factorial design was made by combining two independent variables—oil content and surfactant concentration—and two responses—particle size and percentage of in vitro release. One ideal formula was selected and put through a stability analysis based on the desire function. The properties, stability, in vitro release, and ex vivo penetration of a meloxicam-loaded nanoemulgel produced from the optimised nanoemulsion and HPMC as a gelling agent were examined. Finally, the effectiveness of the anti-inflammatory drug was evaluated and compared to both a placebo and a gel version of the drug. The developed nanoemulgel showed the correct physical characteristics for topical application. Six hours of in vitro release studies were successfully completed. The ex vivo permeability was induced by the nanoemulgel formulations, which demonstrated

an appropriate value for the steady-state transdermal flow (SSTF). Last but not least, the antiinflammatory activity of the created nanoemulgel showed a significant anti-inflammatory impact. Additionally, it has been shown that meloxicam and eucalyptus essential oil combine well and have the power to lessen and combat inflammation.[24]

ii. **Rizg WY. *et al.* (2022):** The objective of this study was to develop anlovastatin (LV), and the essential oil of eucalyptus (Eu oil) nanoemulgel that could be transformed into a nanoemulsion and tested for cytotoxicity against the human chondrosarcoma-3 tongue cancer cell line (HSC3).[25]

iii. **Sultan MH. *et al.* (2022):** The objective of the current study was to create a nanoemulgel formulation of Nigella sativa oil (NSO) that may be used locally to treat periodontal problems. The nanoemulgel formulation was created by combining an NSO-containing nanoemulsion with a methylcellulose gel basis. Using a Box-Behnken statistical design (quadratic model) with 17 runs, the resultant formulation was optimised. On two dependent responses, pH and viscosity, the impacts of independent factors, such as the amounts of water, oil, and polymers, were investigated. The new formulation's stability, antibacterial effectiveness, droplet size, and drug release all underwent further testing.[26]

iv. **Nagaraja S. *et al.* (2021):** Using Acrysol K140 as an oil, Tween 80 as a surfactant, and Transcutol HP as a cosolvent, we developed a lipid-based nanoemulsifying drug delivery system for naringin in an attempt to improve solubility and capitalise on the benefits of nanosizing, such as enhanced cellular penetration.[27]

v. **Eid AM. *et al.* (2021):** Safrole oil was turned into a nanoemulgel using a self-emulsifying procedure. The antibacterial efficacy of safrole oil and safrole nanoemulgel was then assessed against various microorganisms, and the MTS test was used to determine cytotoxicity against Hep3B cancer cell lines.[28]

vi. **Aman RM. *et al.* (2020):** Clove essential oil is one phytochemical that has a variety of biological effects. Research on developing nano topical delivery systems designed to increase the anti-inflammatory action of the oil, however, has not been conducted. In this study, nanoemulgel and nanofibers (NFs), which are controlled release nanoparticulate systems of the oil, were created in order to do this.[29]

1.7.Excipients

i. **Khan R. *et al.* (2022):** This study examines the viability of adopting a nanoformulation technique to create a fulvic acid-based thymoquinone nanoemulsion gel (FTQ-NEG) with improved solubility and absorption. For the o/w nanoemulsion, the excipients, surfactant/co-surfactant, and oil were Tween 80/Transcutol-P and kalonji oil (FTQ-NE).[30]

ii. **Aithal GC. *et al.* (2018):** The spontaneous emulsification method was used to make a nanoemulsion. Water was used as the aqueous phase, 125 g/200 L of quercetin, tween 80, and Carbitol® were used as the surfactant-cosurfactant combination (Smix), and cinnamon oil was used as the oil phase. It was made with Poloxamer 407, which makes up about 23% of the gel in the nanoemulgel.[31]

CHAPTER – 3

RATIONAL OF THE STUDY

The development and evaluation of gentamicin sulphate ophthalmic nanoemulgel is a component of the present study's strategy for treating bacterial eye infections. Gentamicin sulphate is an antibiotic classified as an aminoglycoside. It is a BCS class III medicine with a great solubility and a low biological half-life of two to three hours. Although gentamicin sulphate is available as an ophthalmic solution and ointment, ophthalmic nanoemulsions have been found to have better corneal permeability and residence time. Finding the cosurfactant that performs best with the penetration enhancer is another aim of the study. The cosurfactants are ethanol and PEG400, with tween 80 acting as the surfactant (penetration enhancer).

3.1 ADVANTAGE OF THE RATIONAL

1) Better & viable option for eye infection.
2) Palatable and appropriately formulated.
3) Fewer side effects.
4) Decreases the cost of hospitalization.
5) Cost effective.
6) More affordable and accessible.
7) Averting the mortalities.

Hence the aim of my study is to improve the permeability and corneal residence time of gentamicin sulphate by formulating it as nanoemulsion, thereby to reducing the dosing frequency.

There are numerous drawbacks to topical dose formulations such cream, lotion, and ointment. One of these is stickiness, which causes issues for patients during application and has poor spreading qualities and requires rubbing. Additionally, several issues with formulation stability for hydrophilic drugs were found. Due to these issues with most semisolid preparations, both pharmaceutical and cosmetic preparations have increased their use of gelled formulation. Gel is a colloid that contains 99% liquid and is made up of a macromolecular network of fibres made of a substance that gels and liquids that are held in place by surface tension. Despite the benefits, delivering hydrophobic medicines is a significant challenge. To get around this issue, a gel-based system can integrate a lipophilic medicinal moiety via an emulsion-based approach.

CHAPTER – 4

MATERIAL AND METHODS

4.1. DRUG PROFILE

4.1.1. Introduction:

In 1963, the antibiotic aminoglycoside gentamicin was discovered from Micromonospora purpurea. It is one of the most often prescribed aminoglycosides because of its broad range of functions, reasonable price, and accessibility. Both gram-positive and gram-negative bacteria respond well to gentamicin treatment, however it works best for Pseudomonas aeruginosa and other serious gram-negative infections. Synergy, which occurs when beta-lactams and gentamicin are administered together, provides a further advantage. This synergistic activity may also assist to optimise dose and reduce adverse effects in addition to aiding in the treatment of difficult illnesses.

Despite being well-known and having a variety of therapeutic applications, gentamicin is also associated with harmful side effects, such as nephrotoxicity and ototoxicity, which may limit its use.

Gentamicin Sulfate, an antibiotic belonging to the aminoglycoside family, is created when the actinomycete Micromonospora purpurea develops.

This medication has the potential to either prevent or treat a wide range of bacterial illnesses. Gentamicin is a member of the antibiotic group known as aminoglycosides. It works by halting the growth of microorganisms.

Gentamicin's actions may be able to overcome the resistance of clinical isolates of bacteria to other aminoglycosides.

In conclusion, a variety of aerobic infections in the body are treated with the aminoglycoside gentamicin.

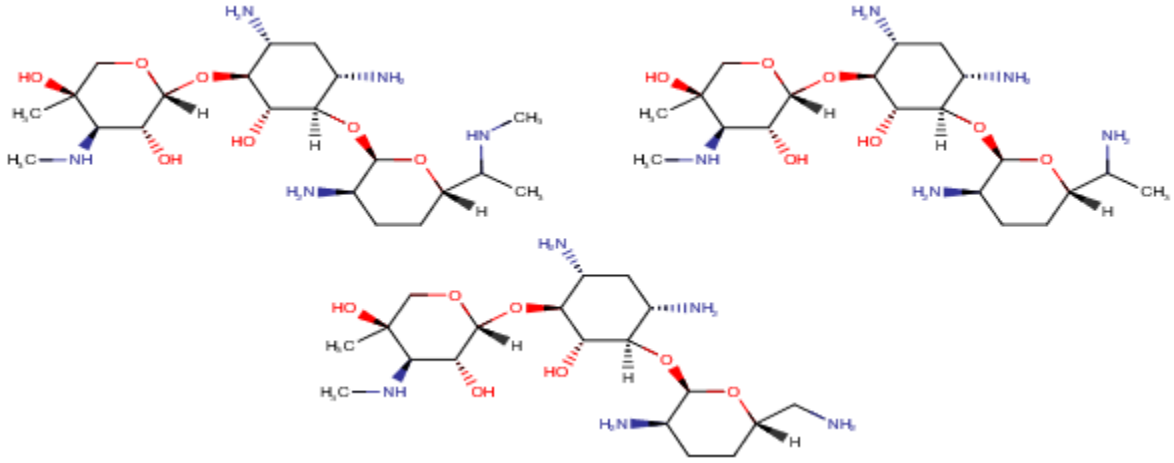
Brand Names- *Gentak, Pred-G, Valisone-G*

Generic Name- Gentamicin

DrugBank Accession Number- DB00798

Type- Small Molecule

Structure-



Chemical Formula- $C_{60}H_{125}N_{15}O_{25}S$

Weight-

Average: 1488.8

Monoisotopic: 1487.869175759

IUPAC NAME-

1. (2R,3R,4R,5R)-2-{[(1S,2S,3R,4S,6R)-4,6-diamino-3-{[(2R,3R,6S)-3-amino-6-(1-aminoethyl)oxan-2-yl]oxy}-2-hydroxycyclohexyl]oxy}-5-methyl-4- methylamino)oxane-3,5-diol;
2. (2R,3R,4R,5R)-2-{[(1S,2S,3R,4S,6R)-4,6-diamino-3-{[(2R,3R,6S)-3-amino-6-(aminomethyl)oxan-2-yl]oxy}-2-hydroxycyclohexyl]oxy}-5-methyl-4-(methylamino)oxane-3,5-diol;
3. (2R,3R,4R,5R)-2-{[(1S,2S,3R,4S,6R)-4,6-diamino-3-{[(2R,3R,6S)-3-amino-6-[1-(methylamino)ethyl]oxan-2-yl]oxy}-2-hydroxycyclohexyl]oxy}-5-methyl-4-(methylamino)oxane-3,5-diol; sulfuric acid

Antibacterial Activity

Gentamicin has been shown to be active against most of the following bacteria, both in vitro and in clinical infections.

2. **Gram-Positive Bacteria**
    - Staphylococcus species

3. **Gram-Negative Bacteria**
    - Citrobacter species
    - Enterobacter species
    - Escherichia coli
    - Klebsiella species
    - Proteus species
    - Serratia species
    - Pseudomonas aeruginosa

CHAPTER – 5

AIM AND OBJECTIVE

AIM: FORMULATION AND EVALUATION OF GENTAMYCIN SULPHATE OPTHALMIC NANOEMULGEL

Objective:

1. To perform the formulation studies of gentamycin sulphate with excipients
2. To formulate the nanoemulsion of gentamycin sulphate using suitable oil, surfactant/co-surfactant.
3. Evaluation of nanoemulsion/nanoemulgel formulation on the basis of size, drug content, *in-vitro* studies etc.
4. Stability studies of nanoemulsion as per ICH guidelines.

CHAPTER – 6

PLAN OF WORK

Step1: Preformulation studies.

1) Identification of drug based on melting point, UV and FTIR spectroscopy.
2) Drug, oil, and Smix compatibility study by
    a) FTIR
    b) DSC
    c) X-RD
3) Interaction drug-excipients and excipients-excipients interaction studies.
4) Determination of solubility of drug in solvent, oil, and Smix.

Step2: **Optimization and Formulation**

1) Optimization Studies
    a) Central Composite Design
    b) Box behnken design
    c) Taguchi design
    d) D-optimal
2) Preparation of phase diagram.
3) Selection of formulation from phase diagram.
4) Formulation methods-
    a) High pressure homogenization
    b) Micro-fluidization
    c) Persuasion method/phase inversion technique
    d) Brute force method

Step 3: Evaluation of nanoemulsion

Physical Evaluation of formulation.

1) Morphological evaluation droplets size.
2) % Transmittance.
3) Refractive index (RI).

4) Dispersibility index
5) Conductivity
6) Viscosity
7) In-vitro permeation studies
8) TEM

Step 4: Formulation of nanoemulgel by gelling agent

Step 5: Evaluation of Nanoemulgel

1) Viscosity
2) Spareability
3) Ocular irritation
4) In-vivo permeation studies
5) In-vitro permeation studies

Step 6: Stability studies

1) Accelerated stability studies

S.N.	**STUDY**	**DURATION**
1	Review of Literature	3 Month
2	Screening and Selection & procurement of drug and excipient	3 Month
3	Preformulation study	3 Month
4	Formulation and optimization of dosage form	3 Month
5	Evaluation of dosage form	3 Month
6	Stability study	6 Month
7	Thesis writing	3 Month
	Total time period of study	**2 Years**

CHAPTER – 7

FUTURE SCOPE

Gentamicin sulphate is an antibiotic belonging to the class of aminoglycoside antibiotic used in treating eye infection. It was BCS class III. It shows low permeability which needs to be improved during formation of nanoemulsion. Gentamicin sulphate is available in market in the form of solution. So, in order to improve the bioavailability of drug, required to formulate as nanoemulsion. The poor permeation of drug is improved by addition of penetration enhancer.

Hence the aim of my study is to improve the permeability and corneal residence time of gentamicin sulphate by formulating it as nanoemulsion, thereby to reducing the dosing frequency.

CHAPTER – 8

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